Summary of Safety and Effectiveness

DEC 2 7 2001

K012183

As required by 21 CFR 807.92, the following 510(k) Summary is provided:

1. **Submitters Information**

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Date Summary Prepared: March 2, 2001

2. **Device Information**

Proprietary Name:	Bayer Diagnostics ADVIA Centaur Toxoplasma IgG
Common Name:	Immunoassay, Toxoplasma Gondii
Device Classification:	Class II 21 CFR 866. 3780

3. **Predicate Device Information**

Name:	Vidas TOXO IgG K922737
Manufacturer:	bioMerieux

4. **Device Description**

Toxoplasma gondii is an intracellular parasitic protozoan that affects birds and mammals, with cats being the primary host. Infection is typically spread by eating raw or undercooked meat containing cysts or by coming in contact with oocyst-infected cat feces. Climate, dietary customs, and presence of cats influence the prevalence of T. gondii, which can vary considerably by geographical location and age. In healthy immunocompetent individuals, infections are usually asymptomatic or subclinical. If toxoplasmosis is diagnosed during the early stages of infection, the disease can be treated effectively with antibiotic therapy.

In pregnant women, T. gondii infection poses a potential threat to the fetus. The risk of a pregnant woman passing infection to the fetus is approximately 25% in the first trimester and increases to approximately 65% in the third trimester.[1] The earlier in the pregnancy that the mother is infected the greater the potential severity of congenital toxoplasmosis. If the fetus becomes infected, the infant may have symptoms such as lymphadenopathy, chorioretinitis, microcephaly and cerebral calcifications. In immunosuppressed populations, such as cancer patients undergoing chemotherapy, transplants recipients, and AIDS patients, T. gondii has emerged as an important opportunistic pathogen leading to severe or fatal infections. The immunosuppressed state of these patients is thought to allow reactivation of a latent infection, and these patients may present symptoms such as headaches, confusion, fever, and focal neurological deficits.

Use of toxoplasma IgG assays has been shown to be a reliable method for establishing immune status and evaluating susceptibility to *T. gondii* infection. The presence of IgG antibodies indicates that the individual has been infected with toxoplasma in the past, but the level of reactivity does not indicate how recently the infection occurred. In the majority of AIDS patients, the IgG response to primary *T. gondii* infection often lacks a significant rise in IgG titers.

5. Statement of Intended Use

The ADVIA Centaur Toxoplasma IgG assay is an IgG antibody capture microparticle direct chemiluminometric immunoassay for the quantitative and qualitative detection of IgG antibodies to the *Toxoplasma gondii* parasite in human serum or plasma (EDTA, heparin) as an aid in the assessment of immune status to toxoplasma in individuals.

6. Summary of Technological Characteristics

The ADVIA Centaur Toxoplasma G assay is an immunoglobulin class-capture sandwich immunoassay using direct, chemiluminometric technology. The anti-human IgG_{Fc} monoclonal antibody is covalently coupled to paramagnetic particles in the Solid Phase. In the Lite Reagent, the purified *T. gondii* antigen is bound to an anti-p30 monoclonal labeled with acridinium ester. Antibody-antigen complexes will form if toxoplasma IgG is present in the sample.

A direct relationship exists between the amount of toxoplasma IgG activity present in the patient sample and the amount of relative light units (RLUs) detected by the system. A result of positive or negative is determined using a clinical cutoff value of 10 IU/mL.

7. Performance Characteristics

Expected Values

The prevalence of IgG antibody to *T. gondii* varies considerably by geographic location and the age of the patient. The following seroprevalence rates for various populations have been reported in the literature::

Location	*Seroprevalence Rate*
Europe	
France, Italy	50–85%, by region
Germany	20–72%, by region
United Kingdom	20%
Japan	24%
Africa	20–65%, by country

S. America	36–82%, by country
N. America	8–38%, by region

In clinical trials, the seropositive rates for IgG antibody to *T. gondii* of samples obtained in the U.S. from pregnant women (N = 494) and low risk and healthy individuals (N = 1224) were 15.0% and 18.6%, respectively.

The distribution of ADVIA Centaur Toxoplasma G classifications observed in the clinical trials are summarized below:

Population	*N*	*Positive*
Pregnant women	494	74 (15.0%)
Random Hospital/Clinical patients	1224	228 (18.6%)
Total	1718	302 (17.6%)

Sensitivity and Specificity

Relative Sensitivity and Specificity

The performance of the ADVIA Centaur Toxoplasma G assay was determined by testing a total of 1804 samples at three U.S. sites. The ADVIA Centaur results were compared to test results generated on a commercially available, automated toxoplasma IgG EIA. Fresh and frozen samples from the mid-Atlantic and Midwest regions of the United States were used. The samples included the following populations: prenatal (N = 494), asymptomatic blood donors (N = 418), asymptomatic hospital patients (N = 806), and 86 patients with confirmed toxoplasma IgG positive status. Of the 1804 specimens tested, 39 were equivocal by either the ADVIA Centaur or the predicate EIA. Discordant results were found on 32 specimens which were further evaluated using other commercially available tests for toxoplasma IgG.

Relative Sensitivity

Using the alternative method, 388 tested positive for toxoplasma IgG antibody. Of the specimens that tested positive, 12 were equivocal, 363 were positive, and 13 were negative using the ADVIA Centaur Toxoplasma G assay. The relative sensitivity was 96.5%.

Relative Specificity

Using the alternative method, 1400 tested negative for toxoplasma IgG antibody. Of the specimens that tested negative, 11 were equivocal, 19 were positive, and 1370 were negative using the ADVIA Centaur Toxoplasma G assay. The relative specificity was 98.6%.

NOTE: Samples giving equivocal results were not included in the calculation of relative sensitivity, relative specificity, and relative agreement.

Relative Sensitivity, Specificity, and Agreement Before Resolution of Discordant Samples

Site	*N*	*Relative Sensitivity (%)*	*Relative Specificity (%)*	*Relative Agreement (%)*
1	804	99.5 (210/211)	98.4 (568/577)	98.7 (778/788)
2	500	94.7 (89/94)	97.7 (384/393)	97.1 (473/487)
3	500	90.1 (64/71)	99.8 (418/419)	98.4 (482/490)
Total	1804	96.5 (363/376)	98.6 (1370/1389)	98.2 (1733/1765)

Relative refers to a direct comparison of ADVIA Centaur Toxoplasma G results to that of a similar assay. No attempt has been made to correlate with disease presence or absence, and no judgement can be made regarding the predicate assay's accuracy to predict toxoplasma disease.

		Predicate Toxoplasma G EIA			
		Positive	Equivocal	Negative	Total
ADVIA	Positive	363	6	19	388
Centaur	Equivocal	12	1	11	24
Toxoplasma	Negative	13	9	1370	1392
G	Total	388	16	1400	1804

Realtive Sensitivity = 96.5% (363/376), 95% CI (Confidence Interval) = 94.16 – 98.15
Relative Specificity = 98.6% (1370/1389), 95% CI = 97.9 – 99.2
Relative Agreement = 98.2% (1733/1765), 95% CI = 97.5 – 98.8

Consensus Testing

Further analysis of the 32 specimens with discordant results was performed using another commercially available test for toxoplasma IgG. Upon retest in duplicate, two Centaur positive specimens were equivocal. Of the thirteen specimens that were negative by ADVIA Centaur and positive by EIA, three were equivocal and three were negative by consensus testing. Of the seventeen specimens that were positive by ADVIA Centaur and negative by EIA, six were equivocal and three were positive by consensus testing.

CDC Panel

A characterized CDC Toxoplasma 1998 Human Serum Panel was obtained from the Centers for Disease Control (CDC) and tested with the ADVIA Centaur Toxoplasma IgG assay. Testing was performed to provide additional information about the performance of the ADVIA Centaur Toxoplasma G assay with a masked characterized panel. Results were submitted to the CDC for their interpretation. This does not imply an endorsement of the assay by the CDC.

The panel consisted of 70 positive and 30 negative specimens as defined by the Dye Test. Of the 70 positives, ADVIA Centaur identified 68 as positive and 2 as equivocal. The two equivocal specimens were aliquots of the same sample. Of the 30 negatives, ADVIA Centaur identified 30 as negative. The ADVIA Centaur Toxoplasma G assay had 98% total agreement with the CDC results. Of the results obtained by the ADVIA Centaur Toxoplasma G assay, there was 97% agreement with the positive specimens and 100% agreement with the negative specimens.

Evaluation of Potentially Interfering Agents

The ADVIA Centaur Toxoplasma G assay was evaluated for potential cross reactivity/interference with 128 viral antibodies and disease state specimens. The negative toxoplasma IgG status of the specimens was verified using alternative EIAs. The table outlines the results obtained on the ADVIA Centaur Toxoplasma G assay.

Disease State	*# of Samples*	*Sample*	*ADVIA Centaur Toxoplasma IgG Results*		
		Type	*Negative*	*Equivocal*	*Positive*
Anti-Mitochondrial Antibodies (AMA)	10	Serum	6	1	3
Anti-Nuclear Antibodies (ANA)	8	Serum	8	0	0
Epstein Barr Virus (EBV) IgG	5	Serum	5	0	0
Flu Vaccine	11	Serum	10	0	0
Heterophilic/HAMA	10	Plasma	10	0	0
Herpes Simplex Virus (HSV) IgG	10	Serum	10	0	0
Measles (Rubeola) IgG	14	Serum	14	0	0
Multiple Myeloma (MM) IgG	10	Serum	9	1	0
Parvovirus B19 IgG	10	Serum & Plasma	10	0	0
Rheumatoid Factor (RF)	12	Serum & Plasma	11	1	0
Syphilis	9	Serum	8	0	1
Varicella Zoster (VZV) IgG	11	Serum	10	1	0
Cytomegalovirus (CMV) IgG	8	Serum & Plasma	8	0	0

Precision

Reproducibility of the ADVIA Centaur Toxoplasma G assay was determined as described in NCCLS protocol EP5-T2.[12] A 5-member panel was assayed two times in two separate daily runs, over a period of 20 days (n = 80). The following results were obtained using one reagent lot and a stored calibration curve:

		Mean Concentration	*Within-run*		*Total***	
Panel Member	*N*	*(IU/mL)*	*SD*	*%CV*	*SD*	*%CV*
Negative Control	80	0.37	0.06	NA*	0.09	NA
Positive Control	80	27.54	0.89	3.2	0.98	3.6
1	80	1.67	0.09	5.2	0.12	7.3
2	80	8.22	0.14	1.7	0.33	4.0
3	80	20.00	0.27	1.3	0.65	3.3

* Not applicable.

** Includes within-run and run-to-run.

System reproducibility was determined by testing a 6 member panel with 3 reagent lots including 5 instruments and 3 sites over multiple days. The panel was assayed three times in each of 40 runs. The following results were obtained:

Panel Member	N	Mean Concentration (IU/mL)	Within-run SD	Within-run %CV	Total** SD	Total** %CV
Negative Control	210	0.20	0.23	NA*	0.25	NA
Positive Control	210	29.91	0.61	2.05	0.75	2.51
1	120	18.32	0.44	2.42	0.53	2.91
2	120	45.02	0.84	1.86	1.12	2.50
3	120	50.57	0.96	1.89	1.15	2.27
4	120	123.71	7.84	6.33	7.88	6.37

* Not applicable.

** Includes within-run and run-to-run.

Standardization

The ADVIA Centaur Toxoplasma G assay is standardized against the World Health Organization (WHO) 3rd International Standard for anti-Toxoplasma Immunoglobulin in human serum. Several dilutions of the WHO standard were evaluated against the calibrators. A representative correlation is shown with slope, y-intercept, correlation coefficient and 95% confidence intervals.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 2 7 2001

Barbara Preisel-Simmons, Ph.D.
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Bayer Corporation
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Re: k012183
Trade/Device Name: Bayer Diagnostics, ADVIA Centaur Toxoplasma IgG Assay
Regulation Number: 21 CFR 866.3780
Regulation Name: Toxoplasma gondii serological reagents
Regulatory Class: Class II
Product Code: LGD
Dated: October 17, 2001
Received: October 30, 2001

Dear Dr. Preisel-Simmons:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

This letter will allow you to begin marketing your device as described in your 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D., M.B.A.
Director
Division of Clinical Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

510(k) Number (if known) K012183

Device Name: ADVIA Centaur Toxoplasma IgG assay

Indications for Use: The ADVIA Centaur Toxoplasma IgG assay is an IgG antibody capture microparticle direct chemiluminometric immunoassay for the quantitative or qualitative detection of IgG antibodies to the *Toxoplasma gondii* parasite in human serum or plasma (EDTA, heparin) using the ADVIA Centaur System. The measurement of Toxoplasma IgG may be used to aid in the assessment of a patient's serological response from individuals including women of childbearing age. This assay may also be utilized with an IgM Toxoplasma result to determine recent serological response to Toxoplasma..

Testing should not be performed as a screening procedure for the general population.

This assay has not been cleared or approved by the FDA for the screening of blood or plasma donors.

Woody Dubois

(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K012183

(PLEASE DO NOT WRITE BELOW THIS LINE--CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDHR, Office of Device Evaluation (ODE)

Prescription Use X OR Over the Counter Use _____
(Per 21 CFR 801.109) **(Optional Format 1-2-96)**